

PART ONE
CONDENSATIONS OF VINYLOGS OF PSEUDO BASES
WITH ACTIVE METHYLENE COMPOUNDS

PART TWO
THE USE OF PYRROLE IN THE SYNTHESIS OF
CERTAIN 1-AZABICYCLO COMPOUNDS

BY

EMMETT H. BURK, JR.

B.S., Arkansas State College, 1942

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1949

URBANA, ILLINOIS

1949

PART ONE
CONDENSATIONS OF VINYLOGS OF PSEUDO BASES
WITH ACTIVE METHYLENE COMPOUNDS

PART TWO
THE USE OF PYRROLE IN THE SYNTHESIS OF
CERTAIN 1-AZABICYCLO COMPOUNDS

BY
EMMETT H. BURK, JR.
B.S., Arkansas State College, 1942

AN ABSTRACT OF A THESIS
SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1949

URBANA, ILLINOIS

1949

ACKNOWLEDGMENT

The author wishes to sincerely thank Dr. Nelson J. Leonard for suggesting these problems, and for his advice and encouragement during the course of their investigation.

The author is also grateful to the University of Illinois for the teaching assistantship in 1947 and 1948.



PART ONE

CONDENSATIONS OF VINYLOGS OF PSEUDO BASES WITH ACTIVE METHYLENE COMPOUNDS

INTRODUCTION

Previous workers have shown that certain pseudo bases in the quinoline and isoquinoline series will react with nitroparaffins to yield condensation products in which the hydroxyl group of the pseudo base has been replaced by the nitroalkyl radical. For a complete list of the reactions attempted see reference 1.

Two general methods for carrying out the reaction have been employed. The first method consisted of the reaction of the pseudo base, previously isolated, with the nitroparaffin in the presence of sodium ethylate. In the second method, the pseudo base was formed *in situ* by the addition of a soluble base to the solution of the appropriate quaternary halide, the nitroparaffin usually being present during the addition of the soluble base.

In order to extend the generality of this reaction, a study of the reaction of several of the common nitroparaffins upon the pseudo bases of acridine and phenanthridine was undertaken.

DISCUSSION OF RESULTS

An alcoholic solution of the pseudo base from acridine was formed by the addition of slightly more than one equivalent of potassium hydroxide to an alcoholic solution of 10-methyl-acridinium iodide. The nitroparaffin was then added to this alcoholic solution of the pseudo base and the resulting solution allowed to stand to complete the reaction. Using this procedure, nitromethane gave the mono-condensation product, 9-nitromethyl-10-methylacridan, with a yield of 62.0% of the theoretical amount. Nitromethane gave the mono-condensa-

tion product, 9-(α -nitroethyl)-10-methylacridan, with a yield of 67.6% of the theoretical amount. 1-Nitropropane gave the mono-condensation product, 9-(α -nitropropyl)-10-methylacridan, with a yield of 50% of the theoretical amount. 2-Nitropropane gave the mono-condensation product, 9-[α -(α -methyl-nitroethyl)]-10-methylacridan, with a yield of 34.6% of the theoretical amount.

In the same manner, the reaction of 10-methylphenanthridinium iodide with the nitroparaffins and potassium hydroxide was investigated. When 50% aqueous ethyl alcohol was used as the solvent for the 10-methylphenanthridinium iodide and nitromethane, an oil separated upon the addition of aqueous sodium hydroxide which could not be crystallized. The picrate of this oil had the composition of the picrate of 9-hydroxy-10-methylphenanthridan. Using ethyl alcohol as the solvent and slightly more than one equivalent of potassium hydroxide, nitromethane gave the mono-condensation product, 9-(α -nitroethyl)-10-methylphenanthridan, with a yield of 34.8% of the theoretical amount. Under these conditions, 1-nitropropane gave the mono-condensation product, 9-(α -nitropropyl)-10-methylphenanthridan, with a yield of 54% of the theoretical amount. Unsuccessful attempts were made to prepare the condensation products from nitromethane and 2-nitropropane.

BIBLIOGRAPHY

- 1 Gerhard Leubner, Thesis, Doctor of Philosophy, University of Illinois, 1948.

PART TWO

THE USE OF PYRROLE IN THE SYNTHESIS OF CERTAIN 1-AZABICYCLO COMPOUNDS

INTRODUCTION

Leonard, Hruda, and Long (1) have prepared pyrrolizi-

dine by the reductive ring-closure of dimethyl γ -nitropimelate. The reaction was shown to proceed through the following intermediates, dimethyl γ -aminopimelate, 5- β -carbomethoxyethyl-2-pyrrolidone, and 3,5-diketopyrrolizidine by the isolation of the latter two intermediates.

Recently Herz, Dittmer, and Cristol (2) have reported the synthesis of diethyl (2-pyrrolmethyl)-malonate by the alkylation of diethyl malonate with 2-dimethylaminomethylpyrrole. A cyclic lactam, derived from diethyl (2-pyrrolmethyl)-acetamidomalonate, was also reported by these authors.

The structural similarity between 5- β -carbomethoxyethyl-2-pyrrolidone and diethyl (2-pyrrolmethyl)-malonate and between 3,5-diketopyrrolizidine and the cyclic lactam from diethyl (2-pyrrolmethyl)-acetamidomalonate, together with the ready availability of the 2-pyrrolmethyl compounds reported by Herz and co-workers, suggested that the reductive ring-closure of the 2-pyrrolmethyl compounds might offer a practical method for the synthesis of 2-substituted pyrrolizidines. For these reasons the study of the synthesis and hydrogenation, over copper chromite catalyst at high temperature and pressure, of a series of substituted diethyl (2-pyrrolmethyl)-malonates was undertaken.

DISCUSSION OF RESULTS

The alkylation of a series of diethyl malonates with the Mannich base, 2-dimethylaminomethylpyrrole, has been accomplished. Using the modified procedure of Albertson and co-workers (3), diethyl malonate was alkylated to give a 43.7% yield of diethyl (2-pyrrolmethyl)-malonate when equivalents of the malonic ester and the Mannich base were employed. If two equivalents of the Mannich base were employed per mole of the malonic ester, a compound was isolated, for which the structure was postulated to be diethyl *bis*-(2-pyrrolmethyl)-malonate, in a 37.8% yield. This material was also obtained from the alkylation of malonic ester with one mole of the Mannich base in a low yield. From the attempted alkylation

of tricarbethoxymethane, diethyl (2-pyrrolylmethyl)-malonate and the diethyl *bis*-(2-pyrrolylmethyl)-malonate were the only compounds isolated, a carbethoxy group having been cleaved during the reaction. Using the modified procedure of Albertson and co-workers on a series of substituted malonic esters, diethyl (2-pyrrolylmethyl)-methylmalonate, yield 55.4%, diethyl (2-pyrrolylmethyl)-phenylmalonate, yield 62.8%, diethyl (2-pyrrolylmethyl)-acetoxymalonate, yield 26.8%, and diethyl (2-pyrrolylmethyl)-benzamidomalonate, yield 84%, were obtained. By the use of the procedure of Howe and co-workers (4), the cyclic lactam of diethyl (2-pyrrolylmethyl)-benzamidomalonate was obtained one time in a 30% yield.

The formation of 2-substituted pyrrolizidines by the hydrogenation of the diethyl (2-pyrrolylmethyl)-malonates over copper chromite catalyst at a high temperature and pressure was investigated. The hydrogenation of diethyl (2-pyrrolylmethyl)-malonate under these conditions gave a 59.4% yield of pyrrolizidine under conditions conducive to hydrogenolysis. A mixture of pyrrolizidine and 2-methylpyrrolizidine was obtained upon decreasing the time of exposure to the catalyst. Diethyl (2-pyrrolylmethyl)-methylmalonate gave a 50% yield of 2-methylpyrrolizidine. A material with the composition of 2-methyl-2-hydroxymethylpyrrolizidine was also obtained in a very low yield. A material, empirical formula $C_{15}H_{23}N$, was obtained in a 75% yield from the hydrogenation of diethyl (2-pyrrolylmethyl)-phenylmalonate. This material has been postulated to be 1-[2-(1-ethylpyrrolidyl)]-2-phenylpropane. A picrate, formed from the base obtained by the hydrogenation of diethyl (2-pyrrolylmethyl)-acetoxymalonate, was shown to be the picrate of 2-methylpyrrolizidine. A mixture of pyrrolizidine and 2-methylpyrrolizidine along with unidentified products was obtained from the hydrogenation of diethyl (2-pyrrolylmethyl)-benzamidomalonate.

BIBLIOGRAPHY

1. Leonard, Hruda, and Long, J. Am. Chem. Soc., **69**, 690 (1947).

2. Herz, Dittmer, and Cristol, *ibid.*, 70, 504 (1948).
3. Albertson, Archer, and Suter, *ibid.*, 66, 500 (1944) ; 67, 36 (1945).
4. Howe, Zambito, Snyder, and Tishler, *ibid.*, 67, 38 (1945).

VITA

The author was born in Jonesboro, Arkansas on February 24, 1921. He attended grammar school there, and was graduated from Champaign High School, Champaign, Illinois, in June, 1938. He entered Arkansas State College in September, 1938. He received his Bachelor of Science degree in June, 1942. After graduation he served in the U. S. Army until March, 1946 when he was released to inactive duty. In June, 1946 he entered the Graduate School at the University of Illinois. From September, 1947 to June, 1948 he was a part-time teaching assistant in organic chemistry.

